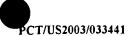


CLAIMS

We claim:

- 1. An isolated nucleic acid molecule of SEQ ID NO:1, wherein G is replaced by C at nucleotide 12.
- 2. The isolated nucleic acid molecule of claim 1 and an isolated nucleic acid molecule of SEQ ID NO:1, wherein the two isolated nucleic acid molecules are forms of a single nucleotide polymorphism in the 5' region of a thymidylate synthase (TS) gene.
- 3. A single-stranded nucleic acid probe that hybridizes to the isolated nucleic acid molecule of claim 1, but not to SEQ ID NO:1.
- 4. The probe of claim 3, wherein the nucleic acid is DNA.
- 5. The probe of claim 3, wherein the probe is detectably labeled.
- 6. A diagnostic kit comprising the probe as defined by claim 3, and/or an allele-specific nucleic acid primer of 8-40 nucleotides specifically hybridizes to and detects the molecule of claim 1, and instructions for use.
- 7. The diagnostic kit of claim 6, wherein the primer is of 12-35 nucleotides.
- 8. The diagnostic kit of claim 6, wherein the primer is of 17-35 nucleotides.
- 9. The diagnostic kit of claim 6, wherein hybridization indicates reduced transcriptional activity of the TS gene, and a corresponding decreased risk of developing a disease.
- 10. The diagnostic kit of claim 6, wherein the disease is cancer or cardiovascular disease.

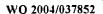


- 11. A method for determining whether an individual has or has a heightened predisposition to cancer or cardiovascular disease, comprising:
 - (a) obtaining a sample from the individual comprising nucleic acid molecules containing a thymidylate synthase gene; and
 - (b) detecting one or more polymorphisms in the TS gene, wherein
 - (i) an individual with an 3R/3R construct in the 5' region of the TS gene more likely has or has a heightened predisposition as compared to an individual with a 3R/3RV, 2R/2R, 2R/3R, or 2R/3RV construct;
 - (ii) an individual with a +6 bp/1494 3' untranslated region

 polymorphism of the TS gene more likely has or has a heightened

 predisposition as compared to an individual with a -6 bp/1494 3'

 untranslated region polymorphism of the TS gene;
 - (iii) an individual with both the 3R/3R construct in the 5' region and a +6 bp/1494 3' untranslated region polymorphism of the TS gene most likely has or has the highest probability of developing cancer or cardiovascular disease (CVD).
- 12. The method of claim 11, wherein an individual with the 3R/3R construct in the 5' region of the TS gene has two active USF consensus sequences in each 3R portion, resulting in greater transcriptional activity as compared to a subject with one active USF sequence in either a 2R construct or a variable 3RV construct.
- 13. The method of claim 11, wherein the detecting step comprises amplifying the portion of the nucleic acid molecule comprising the TS gene.





- 14. The method of claim 13, wherein the amplifying uses the method of polymerase chain reaction.
- 15. The method of claim 11, wherein the determining step comprises sequencing the portion of the nucleic acid molecule comprising the TS gene.
- 16. The method of claim 11, wherein the determining step comprises the use of high throughput screening.
- 17. The method of claim 11, wherein a 3R construct comprises SEQ ID NO:1 and a 3RV construct comprises SEQ ID NO:1, wherein at position 12, G is replaced by C.
- 18. The method of claim 17, wherein the replacement of G by C at position 12 is associated with the efficacy of a chemotherapeutic or anti-CVD drug, and wherein if the replacement of G by C at position 12 has occurred, the chemotherapeutic or anti-CVD drug is more efficacious than if the substitution had not occurred.
- 19. The method of claim 11, wherein the TS gene is derived from bodily fluid of the subject.
- 20. The method of claim 19, wherein the bodily fluid is blood.